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REVIEW ARTICLE

# Lethality by COVID-19 in children: an integrative review

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**Keywords:**
Child,
Coronavirus Infections,
Death.

## Abstract

**Objectives:** To characterize the clinical and epidemiological characteristics of deceased pediatric patients with COVID-19. **Methods:** It was performed an integrative literature review with the keywords "children", "COVID-19" and "death" and the boolean "AND" on the databases SciELO, PubMed, *Literatura Latino-Americana e do Caribe em Ciências da Saúde*, Embase and ScienceDirect. The results were filtered by publication date (January 1st to June 30th) and by language (Portuguese, English and Spanish). The inclusion criteria were: articles with proven or probable pediatric COVID-19 cases and full text in Portuguese, English or Spanish. Articles with no full text available in the above-mentioned languages, non-pediatric population and editorials were excluded. Brazilian data were analyzed based on epidemiological reports from each state of the country. **Results:** 24 articles were analyzed, with a total of 17 deaths among pediatric COVID-19 patients. There was no data available about age of 9 patients and about comorbidities of 14 patients. Brazil had 357 pediatric deaths and 182 of them were on the age group 0-9 years. The most frequent comorbidities were heart disease and diabetes. **Conclusions:** Despite the low distribution of deaths among pediatric COVID-19 patients, it is important to point out that they are still carriers of the disease.

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## INTRODUCTION

COVID-19 (Coronavirus Disease 2019) is caused by SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus 2). This RNA virus has a surface glycoprotein called protein S that plays a key role in viral entry via membrane receptors.[1] Social distancing and wearing face masks are relevant preventive measures, since respiratory transmission of the virus occurs through aerosols and droplets.[2]

Since the recognition of the COVID-19 pandemic by the World Health Organization in March 2020, more than 12.768 million cases of the disease have been confirmed. More than 566,654 people have died of the disease globally. The Americas are topping the list of cases of COVID-19, with more than 6.6 million recorded cases of the disease.[3]

The incidence and death rates of the disease in children have been lower than the numbers reported for adults and the elderly. Children have been considered a population at low risk of COVID-19, since they have accounted for 1-5% of the cases of the disease.[4,5,6] However, it should be mentioned that individuals with infection and mild respiratory and systemic symptoms can transmit the disease, particularly when social distancing measures are not enforced.[7]

This integrative literature review aimed to analyze cases of children and adolescents with COVID-19, the factors potentially associated with deaths in this population, and the death rates reported in this age group.

## METHODS

This integrative literature review analyzed the progress of disease and the death rates reported for children and adolescents diagnosed with COVID-19. Articles were searched in databases SciELO, PubMed, Latin American and Caribbean Health Sciences Literature (LILACS), Embase, and Science Direct. The review included papers published from January 1 to June 30, 2020, after the identification of SARS-CoV-2 as the virus causing the pneumonia outbreak in Wuhan, China.[1,2] The keywords used in the searches were “children”, “COVID-19” and “death”, interconnected by Boolean identifier “AND”. Next, a filter to select papers written in Portuguese, English, or Spanish was applied. On Embase, an additional filter to select only papers published in this database was applied, so that papers available in PubMed were not selected twice. After the subject matter of the articles was identified based on their titles, the abstracts were read and then the full text, based on the inclusion and exclusion criteria described in Figure 1.

Inclusion criteria: (1) studies enrolling children suspected for or diagnosed with COVID-19; (2) full text available in Portuguese, English, or Spanish. Exclusion criteria: (1) articles featuring cases of non-pediatric subjects; (2) articles written in languages other than the three cited above; (3) editorial pieces.

This integrative review was designed following the steps described by Souza[8]:

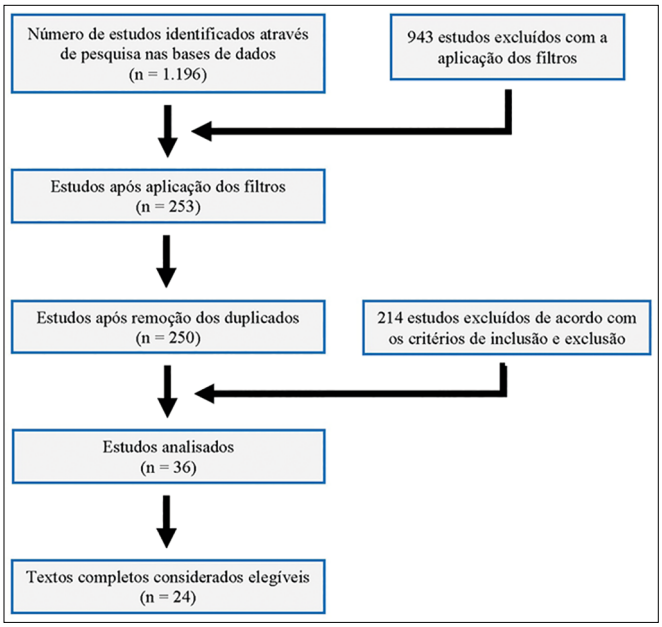


**Figure 1.** Flowchart used in the search for references.

Phase One: Search databases using the abovementioned keywords for articles written in Portuguese, English, or Spanish.

Phase Two: Select articles based on titles and abstracts, in this order.

Phase Three: Read articles to find whether they describe cases of children with the disease and deaths by COVID-19.

Phase Four: The selected articles included systematic reviews, retrospective studies, and epidemiological reports. No clinical trials or experimental studies involving children in the time period of choice were found.

Brazilian data were analyzed based on epidemiological reports published on July 6 by the Secretaries of Health of each Brazilian State and the Ministry of Health. Brazilian States that had not updated their reports by the time the search was made had the data from July 5 included in the study.

## RESULTS

The entire review process was guided by the objective of investigating morbimortality and death rates observed in patients in the pediatric age range. From a total of 1,196 articles found in the databases, 24 were deemed eligible for inclusion in the review.

Information concerning severe and critical cases of disease and deaths of pediatric patients described in the selected articles are summarized in Table 1.

A multicenter epidemiological survey was carried out involving institutions from the United States, United Kingdom, Italy, France, Spain, and Germany, in which the deaths of individuals in the pediatric age range by COVID-19 and other causes were compared. Death rates ranged from 0 to 3.448%,

**Table 1.** Considerations present in the selected articles concerning severe, critical disease, and death of pediatric patients.

| Source | Article Title | Authors | Journal and Date | Considerations/subject |
|---|---|---|---|---|
| Embase | Epidemiological Characteristics of 2143 Pediatric Patients with 2019 Coronavirus Disease in China | Dong Y, Mo X, Hu Y, Qi X, Jiang F, Jiang Z, et al[10] | J Emerg Med April 2020 | Retrospective study with 2143 reporting one death. No statistically significant difference was seen in the distribution of cases between sexes. Subjects aged < 1 and 1-5 years had higher rates of severe and critical disease. A 14-year-old boy died in China of the disease; the article did not provide additional details. |
| PubMed | Systematic review of COVID-19 in children shows milder cases and a better prognosis than adults | Ludvigsson JF[4] | Acta Paediatr March 2020 | Systematic review. Children had milder disease and better outcomes compared with adults. Deaths of pediatric patients were extremely rare. In a study, of the 2143 children diagnosed with or suspected for COVID-19, 5.2% and 0.6% had severe or critical disease, respectively. The prevalence of severe and critical disease was greater in very young children (10.6% in children aged less than a year). Three children with the following comorbidities needed intensive care: bilateral hydronephrosis, chemotherapy for leukemia, and intussusception. Two deaths were reported: a 14-year-old boy, without further details, and a 10-month-old infant with intussusception who died of multiple organ failure. |
| PubMed | Clinical and epidemiological features of 36 children with coronavirus disease 2019 (COVID-19) in Zhejiang, China: an observational cohort study | Qiu H, Wu J, Hong L, Luo Y, Song Q, Chen D[25] | Lancet Infect Dis March 2020 | An observational cohort study with 36 patients and no deaths. Although children had milder involvement than adults, they had to stay in hospital for about 14 days until their PCR tests were normal. |
| Embase | Epidemiology and clinical features of coronavirus disease 2019 in children | Choi et al. (2020)[21] | Clin Exp Pediatr Abril de 2020 | Review article. A study showed that 2.5% and 0.2% of the children had severe or critical disease, respectively. The first pediatric case of severe disease, involving a 13-month-old infant without known comorbidities, was reported in Wuhan, China. Two cases of critical disease: one involving a moderately malnourished child with a history of heart surgery to treat congenital heart disease, and a child with hydronephrosis and nephrolithiasis. One death was reported of an individual aged 10-19 years in China, without further details. |
| LILACS | Epidemiología y manifestaciones clínicas de COVID-19 en niñez | Castellanos E, Zelaya S, Gutiérrez M, Domínguez R[11] | IInstituto Nacional de Salud de El Salvador; April 2020 | This article reports the death of a neonate aged 6 weeks and a 4-year-old child. Newborns and children aged less than a year are more susceptible to developing severe COVID-19. |
| PubMed | Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Infection in Children and Adolescents | Castagnoli R, Votto M, Licari A, Brambilla I, Bruno R, Perlini S, et al[19] | JAMA Pediatr April 2020 | Systematic review including 1065 confirmed cases of COVID-19, individuals of both sexes aged 0-19 years. One case of severe infection in a child aged 13 months. One death of a subject in the 10-19 year-old range. In general, pediatric patients had better outcomes and recovered within one to two weeks from the onset of the disease. Children appear not to be at greater risk of having severe disease based on age or sex. |
| PubMed | Clinical Manifestations of Children with COVID-19: a Systematic Review | Souza TH, Nadal JÁ, Nogueira RJN, Pereira RM, Brandão MB[2] | Pediatr Pulmonol April 2020 | Systematic review. A total of 38 studies (1124 cases of COVID-19 in children) were included, of which 2.1% and 1.2% had severe or critical disease, respectively. One death was reported, involving a 10-month-old infant with intussusception. |
| PubMed | Coronavirus Disease 2019 in Children - United States, February 12-April 2, 2020. | CDC COVID-19 Response Team[23] | MMWR Morb Mortal Wkly Rep April 2020 | Survey about children with COVID 19 in the USA, from Feb. 12 to Apr. 2, 2020. A total of 149760 confirmed cases of the disease, of which 2572 were children (1.7%). Mean age was 11 years (most were aged 10 years or older). Comorbidities included cardiopulmonary disease and immunosuppression. Three deaths were recorded among 345 individuals with comorbidities, although COVID-19 was not confirmed as the cause. |
| PubMed | Novel coronavirus disease (COVID-19) in children | Tezer H, Bedir Demirdağ T[22] | Turk J Med Sci April 2020 | Review. Clinical and epidemiological factors, diagnosis, and treatment. Case study with 295 children, 37 hospitalizations, and three deaths, although COVID-19 was not confirmed as the cause. |
| PubMed | Characterisation of COVID-19 Pandemic in Paediatric Age Group: A Systematic Review | Mustafa NM, Selim LA[18] | J Clin Virol May 2020 | Systematic review and meta-analysis. Children had better outcomes than adults. Death and referral to an intensive care unit rarely occurred. Eight children needed intensive care, one was on immunosuppressants. One neonate born to a mother with COVID-19 died of multiple organ failure and disseminated intravascular coagulation; the cause of death is unclear. No deaths were reported in the other selected articles. However, the authors reported the deaths of a 12-year-old girl in Belgium (Euro News, 2020) and of a 13-year-old boy in the United Kingdom (BBC News, 2020), without further details on comorbidities. |

Continuação **tabela 1.**

| | | | | |
|---|---|---|---|---|
| PubMed | Clinical Characteristics of Children with COVID-19 | Lok Tung Ho C, Oligbu P, Ojubolamo O, Pervaiz M, Oligbu G[20] | AIMS Public Health May 2020 | Literature review; eight articles and 731 pediatric cases of COVID-19 involving subjects of both sexes aged 0-18 years. Dong et al. reported the death of a 14-year-old boy. Current data indicate that children are disproportionately affected by COVID-19 and are more prone to having better outcomes after infection than adults. |
| PubMed | Pediatric COVID-19: Systematic review of the literature | Patel NA[12] | Am J Otolaryngol May 2020 | Systematic review, 2914 confirmed cases of COVID-19 involving individuals of both sexes aged between one day and 17 years. Most of the children had mild disease and good outcomes. A total of 5 deaths were reported: an 11-year-old boy with aplastic anemia; a 10-month-old infant with intussusception and multiple organ failure. Data concerning the other deaths were not available. Mean time of hospitalization ranged from 6.5 to 14 days. Many of the patients requiring referral to an ICU were aged less than a year or had significant underlying medical conditions. |
| PubMed | Children's mortality from COVID-19 compared with all-deaths and other relevant causes of death: epidemiological information for decision-making by parents, teachers, clinicians and policymakers. | Bhopal S, Bagaria J, Bhopal R[9] | Public Health May 2020 | Significance of deaths by COVID-19 in relation to other causes of death in children. USA, UK, Italy, Korea, France, Spain, and Germany Variation: 0 to 3.448% - Mean: 0.333% |
| PubMed | Novel coronavirus infection and children | Cavallo F, Rossi N, Chiarelli F[13] | Acta Biomedica May 2020 | Review including articles published on PubMed reporting cases of children with COVID 19, focusing on epidemiology and symptoms. Two deaths were reported in the articles included in the review of a child aged 10 months and a teen aged 14 years, causes not explained. Conclusion: children develop milder forms of disease. |
| PubMed | Coronavirus Infections in Children Including COVID-19: An Overview of the Epidemiology, Clinical Features, Diagnosis, Treatment and Prevention Options in Children | Zimmermann P, Curtis N[5] | Pediatr Infect Dis J May 2020 | Literature review about the clinical findings and epidemiology of individuals with coronavirus infections, including COVID-19. During the pneumonia outbreak in China, only 2% of the affected individuals were aged less than 19 years. No deaths had been reported until February. |
| PubMed | Coronavirus disease 2019 in children: surprising findings in the midst of a global pandemic | Goldman RD[26] | Can Fam Physician May 2020 | Literature review on the clinical characteristics of COVID-19 in pediatric patients. In Canada, only 5% of the confirmed cases of COVID-19 involved children |
| PubMed | First paediatric COVID-19 associated death in Italy | Mercolini F, Donà D, Girtler Y, Mussner KA, Biban P, Bordugo A, et al[16] | J Paediatr Child Health June 2020 | Case Report. Death by COVID-19 of a 5-year-old girl with mucolipidosis II (mutation in both genes GNPTAB: c.3503_3504delTC). |
| Science Direct | Comparison of Hospitalized Patients with pneumonia caused by COVID-19 and influenza A in children under 5 years | Li Y, Wang H, Wang F, Du H, Liu X, Chen P, et al[27] | Int J Infect Dis June 2020 | Estudo retrospectivo, descritivo, comparando COVID-19 e influenza A em crianças. N116. Não houve óbitos. Casos graves de pneumonia mais frequentes em influenza A. |
| PubMed | Covid-19 in children: A brief overview after three months experience | De Luca et al. (2020)[17] | Paediatr Respir Rev Junho de 2020 | Retrospective descriptive study comparing COVID-19 and Influenza A in children. N116. No deaths. Severe pneumonia was more frequent in individuals with Influenza A. |
| PubMed | COVID-19 in children, pregnancy and neonates: a review of epidemiological and clinical features | Zimmermann P, Curtis N[28] | Pediatr Infect Dis J June 2020 | Literature review comprising 11 articles and 333 children diagnosed with COVID-19. Only one child died in the analyzed articles: a 10-month-old infant with intussusception, in addition to a teenager aged 14 years. Two deaths were reported among pregnant women with COVID-19. |
| PubMed | The early experiences of a single tertiary Italian emergency department treating COVID-19 in children | Brisca G, Ferretti M, Sartoris G, Damasio MB, Buffoni I, Pirlo D, et al[29] | Acta Paediatr June 2020 | Report comprising 24 pediatric patients with COVID-19 in Italy. No deaths. Eleven were hospitalized; none required respiratory support, referral to an ICU, or oxygen therapy. Only three patients had preexisting conditions: a 15-year-old girl with spastic quadriplegia and severe scoliosis; a 7-year-old boy with hydrocephalus and congenital heart disease; and an 18-uear-old girl with systemic lupus erythematosus, obseity, paraplegia, and deep venous thrombosis. |

Continued **table 1.**

| | | | | |
|---|---|---|---|---|
| PubMed | Clinical Characteristics of 182 pediatric COVID-19 patients with different severities and allergic status | Du H, Dong X, Zhang J, Cao Y, Akdis M, Huang P, et al[14] | Allergy June 2020 | Retrospective study with 182 pediatric patient with COVID-19. One death reported, involving a 10-month-old infant with intussusception who developed intestinal necrosis, septic shock, and multiple organ failure. Allergic rhinitis was the most common allergic condition found in the patients, followed by atopic dermatitis, food allergies, asthma, and urticaria. |
| PubMed | What we know so far about Coronavirus Disease 2019 in children: A meta-analysis of 551 laboratory-confirmed cases | Zhang L, Peres TG, Silva MVF, Camargos P[15] | Pediatr Pulmonol June 2020 | Systematic review and meta-analysis. Population of 551 children and adolescents diagnosed with COVID-19 based on lab tests, of which: 18% were asymptomatic, n = 9 had critical/severe disease (only 2 did not have comorbidities; the following comorbidities were described: hydronephrosis [1], leukemia [1], intussusception [1], encephalopathy [1] and congenital heart disease [3]). One death was reported involving a 10-month-old infant with intussusception who developed multiple organ failure. |
| PubMed | Clinical and epidemiological characteristics of pediatric SARS-CoV-2 infections in China: A multicenter case series | Zhang C, Gu J, Chen Q, Deng N, Li J, Huang L, Zhou X[30] | PLoS Med June 2020 | Retrospective observational study. Thirty-four patient aged between one month and 12 years; patients had mild (18%) or moderate (82%) disease. Six (18%) had comorbidities. No deaths reported. |

with a mean value of 0.333%[9]. COVID-19 lethality in children was deemed low.

## DISCUSSION

A total of 30 deaths by COVID-19 of individuals in the pediatric range were reported in the selected articles. However, some overlap was observed between reports, since several studies used the same papers as references.[10] With overlaps discounted, a total of 17 deaths were included in our review:

A 6-week-old male infant, no comorbidities reported, in the United States[11];

A 10-month-old female infant, with intussusception and multiple organ failure[2,4,5,12,13,14,15];

A 4-year-old boy, no comorbidities reported, in El Salvador[11];

A 5-year-old girl, with mucolipidosis II, in Italy[16]; this death was probably reported in another Italian article as the death of an individual aged < 10 years[17];

An 11-year-old boy, with aplastic anemia and a white blood cell count of 1.1 x $10^3$/µL, in Iran[12];

A 12-year-old girl, no comorbidities reported, in Belgium[18];

A 13-year-old boy, no comorbidities reported, in the United Kingdom[18];

A 14-year-old boy, no comorbidities reported, in Hubei Province, China[4,5,10,13,19,20,21].

No details were provided about the deaths of nine patients in the pediatric age range[12,22,23], which makes it harder to verify whether their cases had been reported in prior studies. The cause of death was not confirmed in six cases.

The case of a neonate dead nine days after birth, born to a mother tested positive for COVID-19, in which the child developed multiple organ failure and disseminated intravascular coagulation, was not accounted for as a death caused by SARS-CoV-2 infection in our review, since the cause of death was uncertain.[18]

On July 6, 2020, the number of confirmed cases of COVID-19 in Brazil according to the Ministry of Health was 1,603,055. A total of 602 people died of the disease on that day, and the COVID-19 death toll then was 64,867, which results in a death rate of about 4%. The cases were distributed as follows in the nation's regions: 117,360 (7.3%) in the Midwest; 96,383 (6%) in the South; 289,206 (18%) in the North; 546,956 (34.12%) in the Northeast; and 553,146 (34.5%) in the Southeast.[24] However, the Ministry of Health did not publish the number of deaths per age range.

The data per Brazilian State on the total number of deaths by COVID-19 of individuals of all ages and subjects in the pediatric age range are shown in Table 2. The data reflect the information present in the Epidemiological Reports issued by the State Secretaries of Health on July 6, 2020. Brazilian States that had not updated their reports by the time this article was written had the data from July 5 included. Some State Secretaries of Health did not publish data broken down per age range, which impaired the analysis of death rates of children and adolescents. Such was the case of the States of Mato Grosso, Amapá, Roraima, and Rio de Janeiro. The only State that did not report deaths for individuals in the pediatric age range was Mato Grosso do Sul.

The reports published by the State Secretaries of Health add up to a total of 65,150 deaths by COVID-19. After subtracting the deaths occurred in States in which age was not reported, the number came down to 52,785. From this subset, 352 deaths (0.66%) involved individuals aged 0-19 years. A study by Ludvigsson[4] refers to an article citing 44,972 confirmed cases of COVID-19, including adults and children. In this population, a total of 965 deaths were reported, of which one (0.1%) involved a child. The proportion of deaths of children and adolescents in Brazil in relation to the total number of deaths was greater than the numbers reported in the literature. Yet, deaths in this age range are rare. Unfortunately, the scarce descriptions accompanying these death reports, particularly of comorbidities, hamper the analysis of the factors potentially associated with unfavorable outcomes in this population in Brazil.

**Table 2.** Total Confirmed Deaths and Deaths of Pediatric Patients per Brazilian State.

| Region | State | Total deaths | Deaths in the pediatric age range | | | Comorbidities | Described symptoms | Sex | Skin color | WEBLINK |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | Total | 0-9 years old | 10-19 years old | | | | | |
| SOUTH | PR | 806 | 4 | 1 | 3 | ND | ND | F = 1 | ND M = 3 | http://www.saude.pr.gov.br/sites/default/arquivos_restritos/files/documento/2020-07/INFORME_EPIDEMIOLOGICO_06_07_2020.pdf |
| | RS | 759 | 1 | 1 | 0 | ND | dispneia | M = 1 | preta = 1 | https://admin-planejamento.rs.gov.br/upload/arquivos/202007/06111618-rs-bi--report-diario-5-0-2020-07-06.pdf |
| | SC | 406 | 3 | 1 | 2 | ND | ND | ND | ND | http://www.coronavirus.sc.gov.br/wp-content/uploads/2020/07/boletim-epidemiologico-06-07-2020.pdf |
| MIDWEST | DF | 663 | 2 | 2 | 0 | ND | ND | ND | ND | http://saude.df.gov.br/wp-conteudo/uploads/2020/03/Boletim-COVID_DF-06-de-junho.pdf |
| | GO | 654 | 5 | 2 | 3 | Immunosuppression (1), diabetes (1), cardiovascular disease (2), no comorbidities (1), unknown (1) | ND | F = 2 M = 3 | ND | https://extranet.saude.go.gov.br/pentaho/api/repos/:coronavirus:paineis:painel.wcdf/generatedContent |
| | MS | 122 | 0 | 0 | 0 | - | - | - | - | http://mais.saude.ms.gov.br/sense/app/51c38346-b65d-4f3e-8a80--5111a7a9da76/sheet/ac6353a2-bdf0-46e9-8863-10062ff01d77/state/analysis |
| | MT | 857 | ND | | | ND | ND | ND | ND | http://www.saude.mt.gov.br/upload/noticia/1/arquivo/060720201810-SES-MT-A--boletim-informativo-120---06.07.pdf |
| NORTH | AC | 252 | 5 | 2 | 3 | ND | ffever, coughing, sore throat, dyspnea, others | F = 3 M = 2 | brown = 4 indigenous = 1 | http://covid19.ac.gov.br/ |
| | AM | 2938 | 22 | 12 | 10 | Heart disease, diabetes, hematologic disease, immunosuppression, prematurity, lung disease, kidney disease, Down syndrome | ND | F = 12 M = 10 | yellow = 1 white = 1 indigenous = 2 brown = 17 not informed = 1 | http://www.fvs.am.gov.br/indicador-SalaSituacao_view/60/2 |
| | AP | 442 | ND | | | ND | ND | ND | ND | http://painel.corona.ap.gov.br/ |
| | PA | 5128 | 51 | 31 | 20 | ND | ND | F = 29 M = 22 | ND | https://www.covid-19.pa.gov.br/ |
| | RO | 558 | 2 | 2 | 3 | Chromosomal disease, immunosuppression, end-stage renal disease | ND | F = 3 M = 2 | ND | http://covid19.sesau.ro.gov.br/Home/Estatistica |
| | RR | 368 | ND | | | ND | ND | ND | ND | https://www.saude.rr.gov.br/index.php/informacoesx/coronavirus/informacoes-coronavirus |
| | TO | 224 | 3 | 0 | 3 | ND | ND | ND | ND | http://integra.saude.to.gov.br/covid19/InformacoesEpidemiologicas |
| | AL | 1172 | 16 | 11 | 5 | ND | ND | F = 6 M = 10 | ND | https://www.saude.al.gov.br/wp--content/uploads/2020/07/Informe--Epidemiol%C3%B3gico-COVID-19--n%C2%BA-122-6-7-2020.pdf |
| | BA | 2168 | 16 | 11 | 5 | ND | ND | ND | ND | http://www.saude.ba.gov.br/wp-content/uploads/2020/07/BOLETIM_ELETRONICO_BAHIAN_104___06072020.pdf |
| | CE | 6481 | 39 | 19 | 20 | ND | ND | F = 20 M = 19 | ND | https://coronavirus.ceara.gov.br/boletins/ |

Continued **table 2.**.

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | MA | 2219 | 27 | 14 | 13 | ND | ND | ND | ND | http://www.saude.ma.gov.br/wp-content/uploads/2020/07/BOLETIM-06-07.pdf |
| | PB | 1099 | 7 | 4 | 3 | Hypertension, diabetes, heart disease, neurological disease | ND | F = 2<br>M = 5 | ND | https://superset.plataformatarget.com.br/superset/dashboard/55/ |
| | PE | 5163 | 39 | 27 | 12 | ND | ND | ND | ND | https://12ad4c92-89c7-4218-9e11-0ee136fa4b92.filesusr.com/ugd/3293a8_2338f3e40df3402c9d7b6054f7c03a81.pdf |
| | PI | 809 | 4 | 1 | 3 | ND | ND | ND | ND | hhttps://datastudio.google.com/u/0/reporting/a6dc07e9-4161-4b5a-9f2a-6f9be486e8f9/page/2itOB |
| NORTHEAST | RN | 1254 | 18 | 10 | 8 | Six had comorbidities: obesity (1), chromosomal disease or immune deficiency (3) and diabetes (2); no details on remaining eight | febre, tosse e dispneia | F = 8<br>M = 10 | white:4<br>yellow: 1<br>brown: 9<br>unknown: 4 | https://portalcovid19.saude.rn.gov.br/wp-content/uploads/2020/04/105_boletim_covid19.pdf |
| | SE | 798 | 22 | Deaths reported in the following age ranges: < 1 year (11), 1-4 years (2), 5-14 years (4) and 15-19 years (5) | | ND | ND | ND | ND | https://todoscontraocorona.net.br/wp-content/uploads/2020/07/Boletim-06.07.2020.pdf |
| | ES | 1804 | 10 | 5 | 5 | Kidney (1), heart (1) and lung (1) disease; all others without comorbidities. | fever, diarrhea, coughing, dyspnea | F = 5<br>M = 5 | yellow = 1<br>white = 2<br>brown = 6<br>black = 1 | https://coronavirus.es.gov.br/ |
| SOUTHEAST | MG | 1230 | 4 | 2 | 2 | ND | ND | ND | ND | http://coronavirus.saude.mg.gov.br/images/boletim/07-julho/06-07_Boletim_Epidemiologico_COVID-19.pdf |
| | RJ | 10698 | ND | | | ND | ND | ND | ND | https://coronavirus.rj.gov.br/boletim/boletim-coronavirus-06-07-10-698-obitos-e-121-879-casos-confirmados-no-rj/ |
| | SP | 16078 | 57 | 24 | 33 | 43 had comorbidities (13 aged < 1 year, 4 aged 1-4 years, 3 aged 5-9 years and 23 aged 10-19 years), no further details. | ND | ND | ND | http://www.saude.sp.gov.br/resources/cve-centro-de-vigilancia-epidemiologica/areas-de-vigilancia/doencas-de-transmissao-respiratoria/coronavirus/coronavirus070720_situacao_epidemiologica.pdf |

ND = not described; F = female; M = male; AC = Acre; AL = Alagoas; AP = Amapá; AM = Amazonas; BA = Bahia; CE = Ceará; DF = Distrito Federal; ES = Espírito Santo; GO = Goiás; MA = Maranhão; MT = Mato Grosso; MS = Mato Grosso do Sul; MG = Minas Gerais; PA = Pará; PB = Paraíba; PR = Paraná; PE = Pernambuco; PI = Piauí; RJ = Rio de Janeiro; RN = Rio Grande do Norte; RS = Rio Grande do Sul; RO = Rondônia; RR = Roraima; SC = Santa Catarina; SP = São Paulo; SE = Sergipe; TO = Tocantins.

Table 2 shows the breakdown between age ranges of 0-9 years and 10-19 years. Most of the reports include age range splits in order to facilitate analysis, which however was not the case for Sergipe. Therefore, after subtracting the deaths from this State, we were left with 335 deaths, most of which involving individuals aged 0-9 years (54%; n = 182). The proportion of severe and critical cases described in the literature is higher among younger children, with 10.6%, 7.3%, 4.2%, 4.1%, and 3% for children with ages < 1, 1-5, 6-10, 11-15, and ≥ 16 years.[10,11] Age-based analyses are hampered by the lack of standardization in the division of deaths by age ranges in the data published by the State Secretaries of Health.

In Brazil, the most frequent comorbidities reported between epidemiological weeks 1 (Nov. 29, 2019 to Dec. 4, 2019) and 26 (June 21-27,2020) to affect individuals killed by COVID-19 were heart disease and diabetes. Other important comorbidities, by order of number of associated deaths, were kidney disease, neurological disease, lung disease, immunosuppression, obesity, asthma, liver disease, and hematologic disease. Most of the individuals with comorbidities killed by COVID-19 were aged 60+ years.[24]

There is no clear explanation to why children and adolescents develop milder disease and have lower death rates than adults, although some hypotheses have been considered.[6,10] The

main comorbidities associated with worse outcomes in patients with COVID-19, such as heart disease and diabetes, occur much less frequently in the pediatric population when compared with adults.[6,25] Since schools and daycare centers have been closed in many cities on account of social distancing requirements, children have spent more time at home. Differently from adults, they do not have to go out to work or buy groceries, which significantly decreases their exposure to the virus.[10,11]

Molecular studies about SARS-CoV-2 showed that the angiotensin-converting enzyme 2 (ACE2) receptor works as a cellular receptor for the virus, facilitating viral entry in host cells. This molecule is suspected of presenting lower levels of maturity and function in children, which might potentially lead to less effective interactions between the virus and the host.[10] The immaturity of the immune system in children may also be associated with the differences in cell response between children and adults.[25,26] Another potential protective factor is the higher level of antibodies children possess on account of recurrent respiratory infections commonly seen in individuals in this age group.[11]

## CONCLUSION

Since the WHO declared the COVID-19 outbreak a global pandemic, researchers have been trying to describe the epidemiology of patients with the disease in order to detect the different morbimortality risk profiles. Despite the low occurrence of severe forms of COVID-19 and deaths by the disease in children, it is important to realize that pediatric patients showing mild respiratory and systemic symptoms may transmit the disease if social distancing requirements are not met. Another factor to consider is the scarcity of epidemiological data for different age ranges, which hampers the interpretation of findings related to the disease and decision-making processes tied to it.

## REFERENCES


1. Ou X, Liu Y, Lei X, Li P, Mi D, Ren L, et al. Characterization of spike glycoprotein of SARS-CoV-2 on virus entry and its immune cross-reactivity with SARS-CoV. Nat Commun. 2020 Mar;11(1):1620.
2. Souza TH, Nadal JA, Nogueira RJN, Pereira RM, Brandão MB. Clinical manifestations of children with COVID-19: a systematic review. Pediatr Pulmonol. 2020 Ago;55(8):1892-9.
3. World Health Organization (WHO). Health emergency dashboard [Internet]. Geneva: WHO; 2020; [acesso em 2020 Jul 13]. Disponível em: https://covid19.who.int/
4. Ludvigsson JF. Systematic review of COVID-19 in children shows milder cases and a better prognosis than adults. Acta Paediatr. 2020 Mar;109(6):1088-95.
5. Zimmermann P, Curtis N. Coronavirus infections in children including COVID-19: an overview of the epidemiology, clinical features, diagnosis, treatment and prevention options in children. Pediatr Infect Dis J. 2020 Mai;39(5):355-68.
6. Ramos RT, Silva DCC, Araújo GB, Riedi CA, Ibiapina CC, Bezerra PGM, et al. Aspectos respiratórios da COVID-19 na infância: o que o pediatra precisa saber?. Resid Pediatr. 2020;10(2):1-15.
7. Sant'Anna MFBP. Coronavírus: a pandemia da dor e do despertar da Medicina!. Resid Pediatr. 2020 Abr;10(2):1.
8. Souza MT, Silva MD, Carvalho R. Revisão integrativa: o que é e como fazer. Einstein (São Paulo). 2010;8(1 Pt 1):102-6.
9. Bhopal S, Bagaria J, Bhopal R. Children's mortality from COVID-19 compared with all-deaths and other relevant causes of death: epidemiological information for decision-making by parents, teachers, clinicians and policymakers. Public Health. 2020 Ago;185:19-20.
10. Eastin C, Eastin T. Epidemiological characteristics of 2143 pediatric patients with 2019 coronavirus disease in China. J Emerg Med. 2020 Apr;58(4):712-3.
11. Castellanos E, Zelaya S, Gutiérrez M, Dominguez R. Epidemiología y manifestaciones clínicas de COVID-19 en niñe. Instituto Nacional de Salud de El Salvador. Resid Pediatr. 2020 Abr;4(3):58-68.
12. Patel NA. Pediatric COVID-19: systematic review of the literature. Am J Otolaryngol. 2020 Mai;41(5):102573.
13. Cavallo F, Rossi N, Chiarelli F. Novel coronavirus infection and children. Acta Bio Med [Internet]. 2020 Mai;91(2):172-6.
14. Du H, Dong X, Zhang J, Cao Y, Akdis M, Huang P, et al. Clinical characteristics of 182 pediatric COVID-19 patients with different severities and allergic status. Allergy. 2020 Jun;76(2):510-32.
15. Zhang L, Peres TG, Silva MVF, Camargos P. What we know so far about coronavirus disease 2019 in children: a meta-analysis of 551 laboratory-confirmed cases. Pediatr Pulmonol. 2020 Jun;55:2115-27.
16. Mercolini F, Doná D, Girtler Y, Mussner KA, Biban P, Bordugo A, et al. First paediatric COVID -19 associated death in Italy. J Paediatr Child Health. 2020 Jun 27; [Epub ahead of print]. DOI: https://doi.org./10.1111/pjc.14994
17. De Luca CD, Esposito E, Cristiani L, Mancino E, Nenna R, Cortis E, et al. Covid-19 in children: a brief overview after three months experience. Paediatr Respir Rev. 2020 Jun;35:9-14.
18. Mustafa NM, Selim LA. Characterisation of COVID-19 pandemic in paediatric age group: a systematic review and meta-analysis. J Clin Virol. 2020 Jul;128:104395.
19. Castagnoli R, Votto M, Licari A, Brambilla I, Bruno R, Perlini S, et al. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in children and adolescents: a systematic review. JAMA Pediatr. 2020 Abr;174(9):882-9.
20. Ho CLT, Oligbu P, Ojubolamo O, Pervaiz M, Oligbu G. Clinical characteristics of children with COVID-19. AIMS Public Health. 2020 Mai;7(2):258-73.
21. Choi SH, Kim HW, Kang JM, Kim DH, Cho EY. Epidemiology and clinical features of coronavirus disease 2019 in children. Clin Exp Pediatr. 2020 Abr;63(4):125-32.
22. Tezer H, Bedir DT. Novel coronavirus disease (COVID-19) in children. Turk J Med Sci. 2020 Abr;50(Suppl 1):592-603.
23. Centers for Disease Control and Prevention (CDC). Coronavirus disease 2019 in children - United States, February 12-April 2, 2020. Morb Mortal Wkly Rep. 2020 Abr;69(14):422-6.
24. Ministério da Saúde (BR). Secretaria de Vigilância em Saúde. Boletim Epidemiológico Especial - Doença pelo Coronavírus COVID-19: Semana Epidemiológica 26 (21 a 27/06) [Internet]. Brasília (DF): Ministério da Saúde; 2020; [acesso em 2020 Jul 06]. Disponível em: http://saude.gov.br/images/pdf/2020/July/01/Boletim-epidemiologico-COVID-20-3.pdf
25. Qiu H, Wu J, Hong L, Luo Y, Song Q, Chen D. Clinical and epidemiological features of 36 children with coronavirus disease 2019 (COVID-19) in Zhejiang, China: an observational cohort study. Lancet Infect Dis. 2020 Mar;20(6):689-96.
26. Goldman RD. Coronavirus disease 2019 in children: surprising findings in the midst of a global pandemic. Can Fam Physician. 2020 May;66(5):332-4.
27. Li Y, Wang H, Wang F, Du H, Liu X, Chen P, et al. Comparison of hospitalized patients with pneumonia caused by COVID-19 and influenza A in children under 5 years. Int J Infect Dis. 2020 Jun;98:80-3.
28. Zimmermann P, Curtis N. COVID-19 in children, pregnancy and neonates: a review of epidemiologic and clinical features. Pediatr Infect Dis J. 2020 Jun;39(6):469-77.

29. Brisca G, Ferretti M, Sartoris G, Damasio MB, Buffoni I, Pirlo D, et al. The early experiences of a single tertiary Italian emergency department treating COVID-19 in children. Acta Paediatr. 2020 Jun 30; [Epub ahead of print]. DOI: https://doi.org/10.1111/apa.15451

30. Zhang C, Gu J, Chen Q, Deng N, Li J, Huang L, et al. Clinical and epidemiological characteristics of pediatric SARS-CoV-2 infections in China: a multicenter case series. PLoS Med. 2020 Jun;17(6):e1003130.